

The development of this article was supported by the Campaign for Essential Nutrients, a coalition of Bayer Consumer Health, DSM Nutritional Products, PHARMAVITE LLC., and Pfizer Inc.

Vitamin and Mineral Intake Is Inadequate for Most Americans: What Should We Advise Patients About Supplements?

Jeffrey B. Blumberg, PhD¹; Balz Frei, PhD²; Victor L. Fulgoni III, PhD³;
Connie M. Weaver, PhD⁴; Steven H. Zeisel, MD, PhD⁵

OVERVIEW

Multiple studies have shown that the majority of Americans fall short in obtaining recommended levels of one or more vitamins and minerals in their diets.^{1,2} Some nutrient inadequacies – specifically those involving calcium, potassium, dietary fiber, and vitamin D – were noted as “public health concerns” in the 2015-2020 Dietary Guidelines for Americans released earlier this year.³ In addition, iron intake is listed as a concern for young children and women capable of becoming pregnant or who are pregnant. Data from the US Centers for Disease Control and Prevention (CDC) show that while less than 10% of Americans have outright deficiencies for the nutrients studied, some populations are at higher risk.⁴ While the Dietary Guidelines (and health experts generally) recommend people obtain the nutrients they need from their diet, they also note that dietary supplements can be useful in providing nutrients that are underconsumed or of particular concern in certain population groups.³ Indeed, studies demonstrate that use of vitamin and mineral supplements (VMS) increases nutrient intake,¹ reduces rates of nutrient deficiencies and inadequacies,^{5,6} and is associated with more favorable health and lifestyle choices.⁷

However, insufficient research has been conducted on the effects of dietary supplements on chronic disease outcomes, and the available evidence is conflicting.⁷

Given the evidence for improved outcomes with dietary changes,⁸ physicians should discuss the importance of good nutrition when counseling their patients (and/or refer them to a registered dietitian) and can also consider supplementation in patients who are likely not obtaining required levels of vitamins and minerals from their diet.

AUTHOR DISCLOSURES

In addition to consulting work for the Campaign for Essential Nutrients (CFEN), the authors receive funding support from: USDA ARS grant 58-1950-014 (J Blumberg); Pfizer Consumer Healthcare (B Frei); NIH grant AT008754 (C Weaver); Nestle, and grants from NIH and the University of North Carolina Clinical (DK056350) (S Zeisel). V Fulgoni III, as Senior Vice President of Nutrition Impact LLC, performs consulting and database analyses for various food and beverage companies and related entities.

1. Antioxidants Research Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA
2. Linus Pauling Institute and Department of Biochemistry & Biophysics, Oregon State University, Corvallis, OR
3. Nutrition Impact, LLC, Battle Creek, MI
4. Department of Nutrition Science, Purdue University, West Lafayette, IN
5. Nutrition Research Institute, Department of Nutrition, School of Public Health and School of Medicine University of North Carolina at Chapel Hill, Chapel Hill, NC

INTAKE OF VITAMINS AND MINERALS FALLS BELOW REQUIREMENTS

With the high general awareness of the importance of good nutrition to overall health, many physicians might be surprised to learn that more than 90% of Americans—and therefore, physicians' patients as well—fall short in obtaining even the Estimated Average Requirement (EAR) or Adequate Intake (AI) for at least one vitamin or mineral (micronutrients) in their diets.^{1,2} This deficit is particularly striking considering that EARs are a lower “nutritional bar” compared to the Recommended Dietary Allowances (RDAs)⁹ or Daily Values (DVs) used on food labels¹⁰ (see **BOX at right**).

These inadequate intakes have been shown consistently in analyses of data from the National Health and Nutrition Examination Survey (NHANES)^{1,2,11-13} a yearly assessment by the National Center for Health Statistics of the health and nutrition status of a nationally-representative sample of noninstitutionalized US civilians.¹⁴

The most recently reported NHANES nutrient intake data (2007-2010, $n=16,444$) showed that, among individuals 4 years of age and older, 94% and 89% consume less than the EARs for vitamins D and E, respectively; and 100% and 92% consumed less than the AIs for potassium and choline, respectively, from food alone (**FIGURE 1**).¹

Consistent with these findings, the most recent Dietary Guidelines, released January 6, 2016 by the US Departments of Health and Human Services and of Agriculture, identified potassium, dietary fiber, choline, magnesium, calcium, and vitamins A, D, E, and C as nutrients, “consumed by many individuals in amounts below the Estimated Average Requirement or Adequate Intake levels.”³ The guidelines further recognized vitamin D, calcium, dietary fiber, potassium, and iron (for young children, women capable of becoming pregnant, and women who are pregnant) as, “nutrients of public health concern.”³

AMERICANS AT INCREASED RISK FOR DEFICIENCIES

Inadequate dietary intake of vitamins and minerals can increase the risk of nutritional deficiencies. Deficiencies for many (though not all) vitamins and minerals are defined by cut points in biomarkers, in most cases some level of the micronutrient or a related metabolite in the serum or urine. While less than 10% of the overall US population have nutrition deficiencies, the prevalence

About Dietary Reference Intakes (DRIs)

In the past, the recommended nutrient intakes from the Institute of Medicine (IOM) – the RDAs in the United States and Recommended Nutrient Intakes (RNIs) in Canada – focused primarily on preventing nutritional deficiencies. In 1994, the scope expanded to optimizing health, preventing disease, and avoiding excessive nutrient intakes. These new recommendations, the DRIs, include⁹:

- EARs, the average intake level estimated to meet the requirements of half the healthy individuals in a group (based on life stage and gender)
- RDAs, the average intake sufficient to meet the requirements of 97% to 98% of healthy individuals in a group
- Adequate Intakes (AIs), the recommended average intake level based on approximations or estimates of intake by a group or groups of healthy people and that are assumed to be adequate; used when an RDA has not been determined
- Tolerable Upper Intake Levels (ULs), the highest average daily nutrient intake likely to pose no risk of adverse effects to almost all individuals in the general population

Additionally, Daily Values (DVs), used on food and dietary supplement labels to indicate nutrient content as a percent of daily needs, were established by the US Food and Drug Administration based on the highest of the 1968 and 1989 RDAs for people 4 years of age and older, excluding pregnant and lactating women, and a daily 2000 calorie diet.¹⁰

varies by age, gender and race/ethnicity, and is as high as nearly one-third in certain population groups. The following examples are from the CDC's Second National Report on Biochemical Indicators of Diet and Nutrition⁴:

- 30 million Americans (10.5%) have a vitamin B₆ deficiency, with higher rates among non-Hispanic blacks (15.7%) and those older than age 60 years (16%).⁴ Severe vitamin B₆ deficiency is associated with microcytic anemia, dermatitis (scaling on the lips and cracks at the corners of the mouth), glossitis (swollen tongue), depression and confusion, and weakened immune function.^{15,16} Individuals with borderline vitamin B₆ concentrations or mild deficiency might have no signs or symptoms.

- 23 million Americans (8.1%) have “severe” vitamin D deficiency.* Non-Hispanic blacks (31.1%) and Mexican-Americans (11.3%) are more likely to be vitamin D-deficient compared with non-Hispanic whites (3.6%).⁴ Reports have shown increases in the prevalence of vitamin D deficiency in Americans from 1988 to 2010, with deficiency associated with osteoporosis or bone fracture.^{16–18} Few foods contain vitamin D; people produce it via exposure to sunlight. However, its synthesis is reduced in darkly pigmented skin and with sunscreen use. The potential effects of vitamin D deficiency include rickets (children), osteomalacia and osteoporosis (adults), muscle weakness, and compromised immune function.¹⁹
- 7.5 million women aged 12–49 years (9.5% of that group) have low body iron status, with higher rates among Mexican Americans (13.2%) and non-Hispanic blacks (16.2%). Iron deficiency is linked to reduced physical capacity and poor pregnancy outcomes, and can progress to anemia if not treated.⁴
- Approximately one-third of pregnant women in the

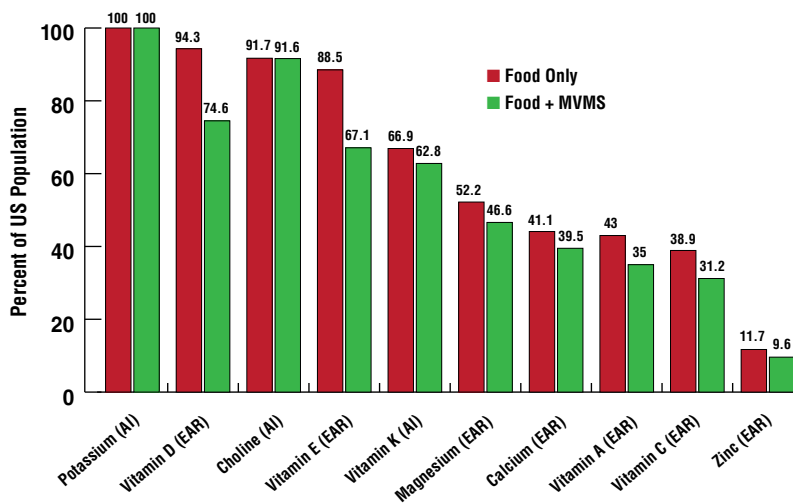
United States are marginally iodine deficient (ie, with intakes bordering on insufficient).^{4,20} Iodine is an essential component of thyroid hormones, which play a key role in normal growth and development and regulate critical enzymes and metabolic processes.⁹

Additional information about the functions and effects of deficiencies of the most common shortfall nutrients is shown in **TABLE 1**.

ADDRESSING MICRONUTRIENT INADEQUACIES

Nutritionists and other health professionals generally advise patients to eat a healthy diet to obtain the required amounts of nutrients and micronutrients. This is a complex challenge to carry out, with many barriers such as inadequate food access, food insecurity, and acculturation. Unfortunately, research shows that relying on providing advice to eat healthier foods does not address nutrient deficits for many Americans. Indeed, the recent Dietary Guidelines state as a goal that people should, “meet nutritional needs primarily through foods,” but also rec-

FIGURE 1. Percent of the US Population Obtaining Less Than the EARs or AIs for Selected Nutrients From Food Alone or Food Plus Multivitamin/Mineral Supplements¹



Abbreviations: AI, adequate intake; EAR, estimated average requirement; MVMS, multivitamin/mineral supplements.

Note: Fewer than 10% of individuals were below the EARs for thiamin, riboflavin, niacin, folic acid, vitamin B6, vitamin B12, iron, copper, phosphorus and selenium (not shown in Figure).¹

Source: Wallace TC, et al. *J Am Coll Nutr.* 2014;33(2):94–102.

* The scientific/medical literature is inconsistent in defining vitamin D deficiency. Here “severe vitamin D deficiency” is defined as a 25-hydroxyvitamin D serum level <30 nmol/L, the cut-off used by the Institute of Medicine (IOM) as the criterion for increased risk for rickets. However, the IOM also defined <50 nmol/L as “insufficient” to maintain bone health, and some scientific reports interpret values below this cut-off as “deficient.” Based on a 50 nmol/L cutoff, the CDC report shows that nearly 90 million Americans (31.7%) have vitamin D deficiency/insufficiency, with higher rates among non-Hispanic blacks (70.6%) and Mexican-Americans (44.2%).⁴

TABLE 1. Vitamins and Minerals Low in Many Americans' Diets: Functions and Effects of Deficiencies^{9,15,16}

Nutrient	Key Functions	Effects of Deficiency
Vitamin A ^{9,15}	Eye and immune function; prenatal and postnatal development; tissue growth, specialization and repair	Night blindness and other vision defects, reduced immune function
Vitamin C ^{9,16}	Most important water-soluble antioxidant, involved in 14 biosynthetic reactions in humans and wound healing	Scurvy, impaired wound healing, weakness, fatigue
Vitamin D ^{9,16}	Bone mineralization, calcium and phosphorous homeostasis; cell division, differentiation and growth; immune function; insulin secretion; blood pressure regulation; neuromuscular function	Rickets in children and osteomalacia in adults; muscle weakness, compromised immune function, bone pain
Vitamin E ⁹	Major fat-soluble antioxidant	Neurologic and eye damage, red blood cell fragility, muscle weakness
Vitamin K ¹⁶	Required for synthesis of a number of proteins involved in normal blood clotting as well as bone formation and cell growth regulation	Impaired blood clotting, potentially manifested as nosebleeds, blood in urine and stools, and intracranial hemorrhaging
Choline ^{9,15}	Serves as methyl donor for various reactions; a component of neurotransmitter acetylcholine and membrane phospholipids	Liver and muscle damage
Calcium ^{15,16}	Major mineral in bones and teeth; intracellular signaling messenger; "on-off" activation of nerve, muscle and other cells; cofactor for a number of enzymes and proteins	Rickets in children; very low bone mineral density (osteoporosis) and increased risk of fractures in adults
Magnesium ⁹	Involved in more than 300 metabolic reactions affecting energy production, DNA and protein synthesis, ion transport, cell signaling; also has structural functions	Reduced levels of calcium and symptomatic hypocalcemia; muscle cramps, neuromuscular hyperexcitability, seizures
Zinc ⁹	Involved in many catalytic, structural and regulatory functions	Growth retardation, hair loss, diarrhea, eye and skin lesions, impaired appetite
Potassium ^{9,16}	An electrolyte, the primary positive ion inside cells, involved in maintaining cell membrane potential	Fatigue, muscle weakness, cramps, cardiac arrhythmias, glucose intolerance

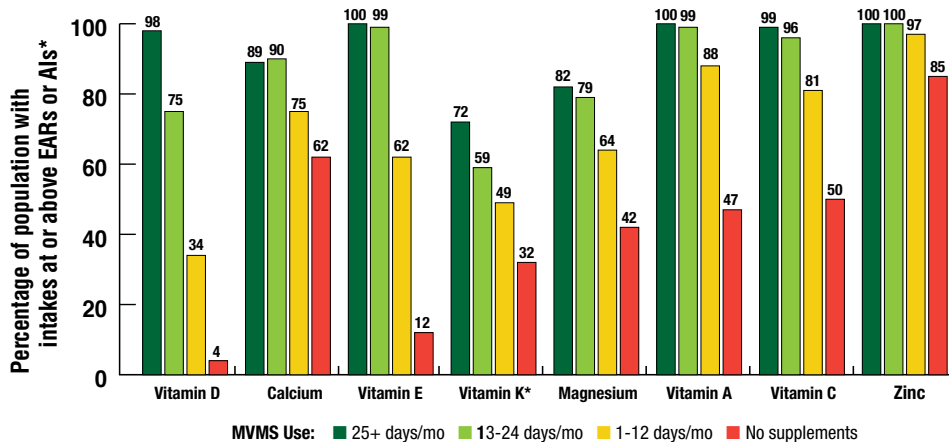
ognize that fortified foods and dietary supplements, "may be useful in providing one or more nutrients that otherwise may be consumed in less than recommended amounts or that are of particular concern for specific population groups."³

Data support the use of VMS to help improve intakes of micronutrients. The NHANES 2007–2010 analysis¹ reported the intake of vitamins and minerals among US residents aged 4 years and older from food alone and from food plus multivitamin/mineral supplements (MVMS). Of the dietary supplements consumed, 51% were MVMS, defined as providing at least 100% of the RDA or AI for nine or more vitamins and minerals

with defined DRI values. The analysis showed that less of the population had intake of vitamins and minerals below many EAR values when nutrient contributions from both food and MVMS were compared to contributions from food alone (**FIGURE 1**).

In **FIGURE 1**, the differences shown between food alone vs food plus MVMS might be less than expected because the comparison was made for the entire NHANES sample (eg, intake of nutrients from food plus MVMS included that from MVMS users and non-users combined [non-users comprised about three-fourths of the 16,444 individuals in the analysis]). Additionally, MVMS users were broadly defined as those

FIGURE 2. Percent of US Adults (19 years or older) With Intake of Micronutrients at or Above EARs or AIs Based on Frequency of Using a Multivitamin/Mineral Dietary Supplement (NHANES 2009-2012)²¹



Abbreviations: AI, adequate intake; EAR, estimated average requirement; MVMS, multivitamin/mineral supplement.

who reported taking a MVMS as infrequently as just once during the 30 days prior to data collection, and so included occasional/sporadic as well as daily users.¹ Finally, some MVMS provide low or no amounts of some nutrients, such as calcium, magnesium, zinc, potassium, and choline. Other analyses have broadly defined “supplements” as those containing vitamins, minerals and/or herbal ingredients.^{11,13} These analytic approaches and definitions can dilute the apparent impact of VMS on micronutrient intake.

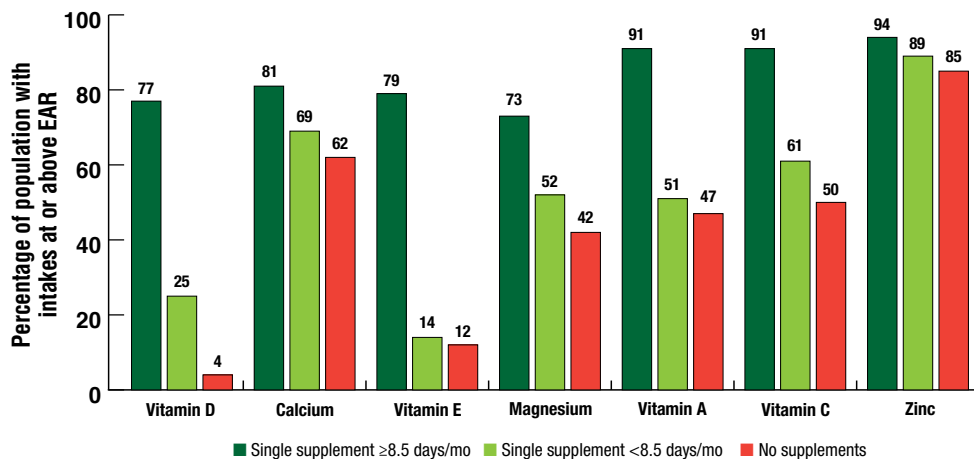
A NEW LOOK AT SUPPLEMENTATION TO IMPROVE NUTRIENT INTAKES

A new analysis²¹ was designed to more closely examine the effects of consumption frequency of VMS, including MVMS and single supplements, on micronutrient intake. NHANES data from 2009 through 2012 (2012 data were the most recent at the time) on nutrient intake from both foods and MVMS in adults 19 years of age and older ($n = 10,698$) were analyzed by quartiles of MVMS consumption frequency over the previous 30 days: none (no supplement of any kind), or MVMS use on 1 to 12 days, 13 to 24 days, or 25 or more days. To ensure adequate sample sizes, the frequencies of single supplement use were categorized as none, <2 days/week (<8.5 days in the previous 30 days), and ≥ 2 days/week (>8.5 days in the previous 30 days). MVMS were de-

defined as supplements providing 100% or more of the RDAs or AIs for 9 or more of the 21 micronutrients with defined DRI values. Single supplements were defined as supplements providing 100% of the RDA or AI for one or more of the same 21 micronutrients. The analysis focused on micronutrients previously shown to be consumed by many Americans in amounts below the EAR or AI levels.

Initial findings show that, for most micronutrients, more frequent MVMS use is clearly and markedly associated with achieving required micronutrient intake (FIGURE 2). For example, for vitamin D, which the Dietary Guidelines identify as a nutrient of public health concern, intake at or above the EAR was achieved by 98%, 75%, 34%, and 4% of adults who, in the previous 30 days, took a MVMS on 25 or more days, 13 to 24 days, 1 to 12 days, and who took no supplement at all, respectively. Choline and potassium (not shown in FIGURE 2) were exceptions, with few adults (less than approximately 10% and 5%, respectively) achieving recommended intake levels regardless of MVMS consumption, likely because those nutrients are found in insignificant amounts in most MVMS products.²¹

Similar results were seen for single supplements (FIGURE 3). For example, for vitamin C, intake at or above the EAR was achieved by 91%, 61% and 50% of adults who, in the previous 30 days, took a single supplement

FIGURE 3. Percent of US Adults (19 years or older) With Micronutrient Intakes at or Above EARs Based on Frequency of Using a Single Dietary Supplement (NHANES 2009-2012)²¹

Abbreviation: EAR, estimated average requirement.

containing vitamin C on 8.5 or more days per month, less than 8.5 days per month, or who took no supplement at all, respectively. Results for choline and vitamin K were not tabulated because very few individuals reported consuming single supplements with those nutrients.²¹

REDUCING DEFICIENCIES IN AMERICANS

A number of reports of vitamin and mineral status of Americans based on biomarker data demonstrate that, while significant portions of the population have or are at risk for deficiencies, rates of deficiencies are lower for VMS users.

For example:

- NHANES data (2001-2006) show the prevalence of vitamin D deficiency, based on serum levels of 25-hydroxyvitamin D <30 nmol/L, is 14% among individuals two or more years of age who do not take a dietary supplement compared with 5% among those who do.⁵
- Based on a standard definition for vitamin B₁₂ deficiency (serum B₁₂ <258 pmol/L or methylmalonic acid >0.21 μmol/L), NHANES data (1999-2002) show 38% of adults age 60 years or older are deficient, but the rate is 30% among those who took any B₁₂-containing VMS in the last 30 days. This definition of deficiency was also associated with significantly increased risks for peripheral neuropathy and disabilities.²²

- NHANES data (2003-2004) show 7% of Americans aged 6 years or older are deficient in vitamin C, based on the standard serum concentration cut off of <11.4 μmol/L. Lower rates of deficiency are found among men and women who used any vitamin C-containing VMS compared to those who did not: 2% (both genders) vs 16% and 11%, respectively).⁶
- NHANES data (2003-2006) show that while only 1% of Americans aged 20 years or older have serum levels of vitamin E meeting the criterion for clinical deficiency (α-tocopherol <12 μmol/L), 81% of dietary supplement nonusers have vitamin E “inadequacy” compared with 46% of users. In this analysis, vitamin E inadequacy was defined as a serum α-tocopherol level below that associated with consuming the EAR and with the lowest mortality rate in a major interventional trial (<30 μmol/L).^{23,24}

Interestingly, supplement users obtain more vitamins and minerals from foods than non-users,^{2,12} so it does not appear that supplements are primarily used to compensate for poor dietary habits.¹ VMS use is also associated with other positive lifestyle behaviors, including moderate alcohol use, more exercise, smoking abstinence, and having health insurance.⁷

Beyond nutritional deficiencies, low intake of vitamins and minerals may be associated with subopti-

mal health. Indeed, as noted in the Box, the concept of optimizing health is a major underpinning for the 1994 shift, from the RDAs to the DRIs for nutrients.⁹ The CDC's Second National Report on Biochemical Indicators of Diet and Nutrition notes⁴:

"...recent findings have determined that less than optimal biochemical concentrations (representing suboptimal status) have been associated with risks of adverse health effects. These health effects include cardiovascular disease, stroke, impaired cognitive function, cancer, eye diseases, poor bone health, and other conditions."

CONCLUSION

Over the past several years, some studies have fueled a debate over the role of VMS in helping to prevent various chronic diseases. While the resulting media headlines and hype may cause confusion, it is important not to lose sight of what vitamins and minerals are: essential nutrients. A vast body of scientific evidence has established the indispensable biochemical and physiological functions of vitamins and minerals as well as the specific amounts needed.

Further research—especially long-term epidemiological studies—is needed on the effects of VMS on chronic disease risk; the findings could also help address some of the challenges identified in using chronic disease endpoints to set DRI values.²⁵ Nevertheless, the collective evidence to date indicates that many Americans are obtaining less than the required amounts of a number of vitamins and minerals. In turn, nutritional deficiencies and insufficiencies can have health consequences. The evidence further shows that VMS use is associated with higher micronutrient intakes and lower rates of deficiencies and inadequacies. Physicians and other health professionals should consider this when counseling their patients, and recommend ways to improve their diets, with VMS considered for patients who are likely not obtaining required levels of vitamins and minerals from their diets. ●

REFERENCES

- Wallace TC, McBurney M, Fulgoni VL 3rd. Multivitamin/mineral supplement contribution to micronutrient intakes in the United States, 2007-2010. *J Am Coll Nutr*. 2014;33(2):94-102.
- Bailey RL, Fulgoni VL 3rd, Keast DR, Dwyer JT. Examination of vitamin intakes among US adults by dietary supplement use. *J Acad Nutr Diet*. 2012;112(5):657-63.
- U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015 – 2020 Dietary Guidelines for Americans. 8th Edition. December 2015. Available at <http://health.gov/dietaryguidelines/2015/guidelines/>.
- Centers for Disease Control. Second National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population. Available at http://www.cdc.gov/nutritionreport/pdf/4Page_%202nd%20Nutrition%20Report_508_032912.pdf. Accessed November 30, 2015.
- Ganji V, Zhang X, Tangpricha V. Serum 25-hydroxyvitamin D concentrations and prevalence estimates of hypovitaminosis D in the U.S. population based on assay-adjusted data. *J Nutr*. 2012;142(3):498-507.
- Schleicher RL, Carroll MD, Ford ES, Lacher DA. Serum vitamin C and the prevalence of vitamin C deficiency in the United States: 2003-2004 National Health and Nutrition Examination Survey (NHANES). *Am J Clin Nutr*. 2009; 90(5):1252-63.
- Bailey RL, Gahche JJ, Miller PE, Thomas PR, Dwyer JT. Why US adults use dietary supplements. *JAMA Intern Med*. 2013;113(5):355-61.
- Knoops KT, de Groot LC, Kromhout D, Perrin AE, et al. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. *JAMA*. 2004;292(12):1433-1439.
- Otten JJ, Hellwig JP, Meyers LD, eds. Dietary Reference Intakes: The Essential Guide to Nutrient Requirements. Washington, DC: The National Academies Press; 2006. Available at http://www.nal.usda.gov/fnic/DRI/Essential_Guide/DRIEssentialGuideNutReq.pdf. Accessed December 22, 2015.
- National Institutes of Health, Dietary Supplement Database. Daily Value. Available at: <http://www.dslid.nlm.nih.gov/dslid/dailyvalue.jsp>. Accessed March 17, 2016.
- Fulgoni VL 3rd, Keast DR, Bailey RL, Dwyer J. Foods, fortificants, and supplements: Where do Americans get their nutrients? *J Nutr*. 2011;141(10):1847-54.
- Bailey RL, Fulgoni VL 3rd, Keast DR, Dwyer JT. Dietary supplement use is associated with higher intakes of minerals from food sources. *Am J Clin Nutr*. 2011;94(5):1376-81.
- Agarwal S, Reider C, Brooks JR, Fulgoni VL 3rd. Comparison of prevalence of inadequate nutrient intake based on body weight status of adults in the United States: an analysis of NHANES 2001-2008. *J Am Coll Nutr*. 2015;34(2):126-34
- Centers for Disease Control and Prevention, National Center for Health Statistics. About the National Health and Nutrition Examination survey. Available at: http://www.cdc.gov/nchs/nhanes/nhanes2011-2012/overview_g.htm. Accessed March 29, 2016.
- Ross CA, Caballero B, Cousins RJ, Tucker KL, Ziegler TR, eds. Modern Nutrition in Health and Disease. 11th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2014.
- Oregon State University. Linus Pauling Institute. Micronutrient Information Center. Available at: <http://lpi.oregonstate.edu/mic>. Accessed November 3, 2015.
- Huang KE, Milliron BJ, Davis SA, Feldman SR. Surge in US outpatient vitamin D deficiency diagnoses: National Ambulatory Medical Care Survey analysis. *South Med J*. 2014;107(4):214-7.
- Ginde AA, Liu MC, Camargo CA Jr. Demographic differences and

- trends of vitamin D insufficiency in the US population, 1988-2004. *Arch Intern Med.* 2009;169(6):626-32
19. Holick MF. Vitamin D deficiency. *N Eng J Med.* 2007;357(3):266-81.
 20. American Academy of Pediatrics Council on Environmental Health, Rogan WJ, Paulson JA, et al. Policy Statement: Iodine deficiency, pollutant chemicals, and the thyroid: new information on an old problem. *Pediatrics.* 2014;133(6):1163-6.
 21. Blumberg J, Frei B, Fulgoni V, Weaver C, Zeisel S. The impact of frequency of vitamin and mineral supplement consumption on micronutrient intakes and biomarkers of nutrient and health status in the United States, 2001-2012. Data on file, Campaign for Essential Nutrient member companies Bayer HealthCare LLC, DSM Nutritional Products and PHARMAVITE LLC. These CFEN members did not direct the analysis or the interpretation of the data. Pfizer was not a sponsor of the study.
 22. Oberlin BS, Tangney CC, Gustashaw KA, Rasmussen HE. Vitamin B12 deficiency in relation to functional disabilities. *Nutrients.* 2013;5(11):4462-75.
 23. McBurney MI, Yu EA, Ciappio ED, Bird JK, Eggersdorfer M, Mehta S (2015) Suboptimal serum α -tocopherol concentrations observed among younger adults and those depending exclusively upon food sources, NHANES 2003-2006. *PLoS ONE* 10(8): e0135510. doi:10.1371/journal.
 24. Wright ME, Lawson KA, Weinstein SJ, et al. Higher baseline serum concentrations of vitamin E are associated with lower total and cause-specific mortality in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Am J Clin Nutr.* 2006;84: 1200-7.
 25. Office of Disease Prevention and Health Promotion. U.S. and Canadian Dietary Reference Intakes (DRI) Committees. Workshop: Options for Consideration of Chronic Disease Endpoints for Dietary Reference Intakes. Available at: <http://health.gov/dietaryguidelines/dri/>. Accessed December 23, 2015.